

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:280279 CAPLUS

DOCUMENT NUMBER: 120:280279

TITLE: Intracellular delivery of biochemical agents
conjugated with peptides

INVENTOR(S): Summer-Smith, Martin; **Barnett, Richard W.;**
Reid, Lorne S.; Twist, Michael

PATENT ASSIGNEE(S): Allelix Biopharmaceuticals Inc., Can.

SOURCE: Can. Pat. Appl., 19 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2094658	AA	19931024	CA 1993 2094658	19930422
PRIORITY APPLN. INFO.:			US 1992-872396	19920423
AB The intracellular delivery of biochem. agents, such as therapeutic peptides and oligonucleotides, is facilitated by a carrier peptide coupled therewith. The carrier peptide consists desirably of pos. charged D-amino acids. Acetyl-[D-Arg]9-NH2 (I) was prepd. by conventional solid phase synthesis using p-methylbenzylhydramine resin as solid support. The uptake of I by cultured HeLa cells after 24 hs was 25.67%.				

L6 ANSWER 33 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:186951 BIOSIS

DOCUMENT NUMBER: PREV199799486154

TITLE: Mutant EGFR is over-expressed in carcinoma of the prostate.

AUTHOR(S): Olapade-Elapopa, E. O. (1); Horsburgh, T.; Mackay, E. H.; Terry, T. R.; Moscatello, D.; Wong, A.; Habib, F. K.

CORPORATE SOURCE: (1) Urology Dep., Leicester General Hosp., Leicester UK

SOURCE: FASEB Journal, (1997) Vol. 11, No. 3, pp. A564.

Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 97 New Orleans, Louisiana, USA April 6-9, 1997

ISSN: 0892-6638.

DOCUMENT TYPE: Conference; Abstract

LANGUAGE: English

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6 ANSWER 29 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:196855 BIOSIS
DOCUMENT NUMBER: PREV199800196855
TITLE: MR1scFvPE38KDEL (MR1), a single chain immunotoxin for the
treatment of tumors expressing EGFRvIII a deletion
mutation
of the EGFR.
AUTHOR(S): Archer, G. E. (1); Fuchs, H. E.; Sampson, J. H.;
Wikstrand, C. J.; Lorimer, I.; Pastan, I.; Bigner, D. D.
CORPORATE SOURCE: (1) Duke Univ., Durham, NC 27710 USA
SOURCE: Proceedings of the American Association for Cancer
Research
Annual Meeting, (March, 1998) Vol. 39, pp. 438-439.
Meeting Info.: 39th Annual Meeting of the American
Association for Cancer Research New Orleans, Louisiana,
USA
March 28-April 1, 1998 American Association for Cancer
Research
. ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 27 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1999:185012 BIOSIS

DOCUMENT NUMBER: PREV199900185012

TITLE: Identification of small peptidic ligands to the
cancer-specific tumor marker EGFRvIII by phage display.

AUTHOR(S): Campa, M. J.; Vinson, E. N.; Pegram, C. N.; Bigner, D. D.;
Patz, E. F., Jr.

CORPORATE SOURCE: Duke Univ. Med. Cent., Durham, NC 27710 USA

SOURCE: Proceedings of the American Association for Cancer
Research

Annual Meeting, (March, 1999) Vol. 40, pp. 484.

Meeting Info.: 90th Annual Meeting of the American
Association for Cancer Research Philadelphia,

Pennsylvania,

USA April 10-14, 1999 American Association for Cancer
Research

. ISSN: 0197-016X.

DOCUMENT TYPE:

Conference

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L6 ANSWER 34 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:414835 BIOSIS

DOCUMENT NUMBER: PREV199699137191

TITLE: Transformation and altered signal transduction by a naturally occurring mutant EGF receptor.

AUTHOR(S): Moscatello, David K.; Montgomery, R. Bruce; Sundareshan, Padma; McDanel, Heather; Wong, Michael Y.; Wong, Albert J. (1)

CORPORATE SOURCE: (1) Dep. Pharmacol., Jefferson Cancer Inst., Thomas Jefferson University, Philadelphia, PA 19107 USA

SOURCE: Oncogene, (1996) Vol. 13, No. 1, pp. 85-96.
ISSN: 0950-9232.

DOCUMENT TYPE: Article

LANGUAGE: English

AB An amino-truncated variant form of the epidermal growth factor receptor (EGFRvIII) has been identified in human brain, breast, lung and ovarian tumors. We have found that overexpression of this mutant EGF receptor in NIH3T3 cells results in transformation as a result of the activation of the receptor kinase via ligand-independent dimerization. Transformation was correlated with tyrosine phosphorylation of only a subset of the proteins observed in cells overexpressing the normal EGF receptor. This suggested that further studies on cells expressing the EGFRvIII might provide insights into the pathways most relevant to transformation. In clones expressing high levels of mutant EGF receptor, the levels of both Grb2 and SHC were decreased. Despite this decrease, much of the endogenous Grb2 immunoprecipitated with EGFRvIII. Interestingly, no increase in ras-GTP loading was found in clones expressing the EGFRvIII and MAP kinase assays indicated only a small increase in activity. These results indicate that high-level expression of the EGFRvIII induces down-regulation of the ras-MAP kinase pathway and that other components involved in EGF receptor signal transduction may play a greater role in neoplastic transformation by the EGFRvIII.

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ACCESSION NUMBER: 1998:194317 BIOSIS
DOCUMENT NUMBER: PREV199800194317
TITLE: Directed evolution of higher affinity single chain Fv
antibodies specific for the mutant EGF receptor EGFRvIII.
AUTHOR(S): Lorimer, I. A. J. (1)
CORPORATE SOURCE: (1) Ottawa Regional Cancer Cent., Cancer Res. Group,
Ottawa, ON K1H 8L6 Canada
SOURCE: Proceedings of the American Association for Cancer
Research
Annual Meeting, (March, 1998) Vol. 39, pp. 65.
Meeting Info.: 89th Annual Meeting of the American
Association for Cancer Research New Orleans, Louisiana,
USA
March 28-April 1, 1998 American Association for Cancer
Research
. ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 28 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1998:343924 BIOSIS

DOCUMENT NUMBER: PREV199800343924

TITLE: Distinct saturable pathways for the endocytosis of different tyrosine motifs.

AUTHOR(S): Warren, Robin A.; Green, Frank A.; Stenberg, Paula E.; Enns, Caroline A. (1)

CORPORATE SOURCE: (1) Dep. Cell Developmental Biol., Oregon Health Sci. Univ., Portland, OR 97201-3098 USA

SOURCE: Journal of Biological Chemistry, (July 3, 1998) Vol. 273, No. 27, pp. 17056-17063.
ISSN: 0021-9258.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Endocytosis of surface proteins through clathrin-coated pits requires an internalization signal in the cytoplasmic domain. Two types of internalization signal have been described: one requiring a tyrosine as the critical residue (tyrosine-based motif), and the other consisting of either two consecutive leucines or an isoleucine and leucine (dileucine motif). Although it seems that these signals are necessary and sufficient for endocytic targeting, the mechanism of recognition is not well understood. To examine this question, tetracycline-repressible cell lines were used to overexpress one of several receptors bearing a

tyrosine-based internalization signal. By measuring the rates of endocytosis for either the overexpressed receptor, or that of other endogenous receptors, we

were able to show that the endocytosis of identical receptors could be saturated, but a complete lack of competition exists between the transferrin receptor (TfR), the low-density lipoprotein receptor, and

the epidermal growth factor receptor. Overexpression of any one of these receptors resulted in its redistribution toward the cell surface,

implying that entry into coated pits is limited. During high levels of TfR expression, however, a significant increase in the amount of surface Lamp1, but not low-density lipoprotein receptor, epidermal growth factor receptor, or Lamp2, is detected. This suggests that Lamp1 and TfR compete for the same endocytic sites. Together, these results support the idea that there are at least three distinct saturable components involved in clathrin-mediated endocytosis.

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ACCESSION NUMBER: 1995:395125 BIOSIS

DOCUMENT NUMBER: PREV199598409425

TITLE: Monoclonal antibodies against EGFRvIII are tumor specific and react with breast and lung carcinomas and malignant gliomas.

AUTHOR(S): Wikstrand, Carol J.; Hale, Laura P.; Batra, Surinder K.; Hill, M. Leslie; Humphrey, Peter A.; Kurpad, Shekar N.; McLendon, Roger E.; Moscatello, David; Pegram, Charles N.; Reist, Craig J.; Traweek, S. Thomas; Wong, Albert J.; Zalutsky, Michael R.; Bigner, Darell D. (1)

CORPORATE SOURCE: (1) Duke Univ. Med. Cent., Pathol. Dep., Box 3156, Durham, NC 27710 USA

SOURCE: Cancer Research, (1995) Vol. 55, No. 14, pp. 3140-3148.
ISSN: 0008-5472.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Despite molecular biological advances in understanding human cancers, translation into therapy has been less forthcoming; targeting neoplastic cells still requires that tumor-specific markers, preferably those on the cell surface, be identified. The epidermal growth factor receptor (EGFR) exists in a deletion-mutant form, EGFRvIII, which has been identified by genetic and immunological means in a subset of gliomas and non-small cell lung carcinomas. Specific polyvalent antisera to the extracellular

portion

of the variant were readily induced, but immunization using a synthetic linear peptide representing the unique EGFRvIII primary sequence has been unsuccessful in mice or macaques. We report here five specific monoclonal antibodies (mAbs) developed through longterm immunization protocols using the EGFRvIII-specific synthetic peptide and the intact variant in different formats that maintained secondary and tertiary conformation. These mAbs identify the EGFRvIII on the cell surface with relatively high affinity (K_A range, 0.13 to 2.5 times 10^{-9} M $^{-1}$) by live cell Scatchard analysis. These mAbs are specific for EGFRvIII as determined by RIA, ELISA, Western blot, analytical flow cytometry, autophosphorylation, and immunohistochemistry. Isolating specific mAbs enabled us to analyze

normal

and neoplastic human tissue and establish that EGFRvIII is truly tumor specific for subsets of breast carcinomas and for previously reported non-small cell lung carcinomas and gliomas. Also, this receptor is not expressed by any normal human tissues thus far examined, including elements of the peripheral, central nervous, and lymphoid systems. With mAbs, we identified a higher incidence of EGFRvIII positivity in gliomas than previously described and identified an EGFRvIII-positive subset of breast tumors; also, we observed that the EGFRvIII epitope is not expressed in normal tissues, and we demonstrated the localizing and therapeutic potential of the mAbs for tumors expressing this epitope. Our observations strongly warrant development of this mAb-antigen system as therapy for breast, lung, and central nervous system tumors.

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